CLAIMS

5

1. Use of a compound of formula (I):

in which:

(I)

10

15

25

30

A is a 6-membered ring optionally containing a double bond and optionally containing an oxygen atom or NR group in the ring;

R is hydrogen or C₁₋₆ alkyl;

R¹ and R² are independently, C₁₋₆ alkyl or C₃₋₆ cycloalkyl both of which can optionally contain one or more O, S or NR³ groups, or R¹ and R² together with the nitrogen atom to which they are attached form a 3,4-dihydroisoquinoline ring or a 5- or 6-membered saturated ring optionally containing a further O, S or N atom and optionally substituted by a group -(CH₂)_p-R⁶ where p is 0 to 3 and R⁶ is C₁₋₆ alkyl, CONR⁷R⁸ where R⁷ and R⁸ are independently hydrogen, C₁₋₆ alkyl which can optionally contain one or more O, S or NR³ groups, or together with the nitrogen atom to which they are attached form a 5- or 6membered saturated ring optionally containing a further O, S or NR³ group; or R⁶ is a 4 to 7-membered saturated ring optionally containing one or more O, S or N atoms, or an aryl or heteroaryl group containing one to four heteroatoms selected from O, S or N, the saturated ring, aryl and heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR⁷R⁸, SO₂NR⁷R⁸, SO₂R³. trifluoromethyl, NHSO₂R³, NHCOR³, C₁₋₆ alkyl, C₁₋₆ alkoxy, SR³ or NR⁹R¹⁰ where R⁹ and R¹⁰ are independently hydrogen, C₁₋₆ alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR³ group;

5

20

R³ is hydrogen or C₁₋₆ alkyl;

R⁴ is hydrogen or C₁₋₆ alkyl;

R⁵ is hydrogen, C₁₋₆ alkyl or C₃₋₆ cycloalkyl both of which can optionally contain one or more O, S or NR³ groups or R⁵ is aryl or a 5- or 6-membered heteroaryl group containing one or two heteroatoms selected from O, S or N, the aryl and heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR⁷R⁸, SO₂NR⁷R⁸, SO₂R³, trifluoromethyl, NHSO₂R³, NHCOR³, C₁₋₆ alkyl, C₁₋₆ alkoxy, SR³ or NR⁹R¹⁰ where R⁹ and R¹⁰ are independently hydrogen, C₁₋₆ alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR³ group;

or R⁴ and R⁵ together form a 5- or 6-membered saturated ring optionally containing a further O, S or NR³ group and optionally substituted by, C₁₋₆ alkyl;

and pharmaceutically acceptable salts or solvates thereof, in the manufacture of a medicament for use in the inhibition of Cathepsin S in a warm blooded animal, such as man.

- 2. Use according to claim 1 in which A is a cyclohexane ring.
- 3. Use according to claim 1 or 2 in which R¹ and R² together with the nitrogen atom to which they are attached form an unsubstituted morpholine ring or a piperidine ring substituted by a group –(CH₂)_p-R⁶ where p and R⁶ are as defined in claim 1
 - 4. Use according to any one of claims 1 to 3 in which R³ is hydrogen.
- 5. Use according to any one of claims 1 to 4 in which R⁴ is hydrogen.
 - 6. Use according to any one of claims 1 to 5 in which R^5 is hydrogen or phenyl optionally substituted by C_{1-6} alkyl or C_{1-6} alkoxy.
- 7. Use according to any one of claims 1 to 6 where the compound of formula (I) is selected from:

- (1R,2R)-N-[Cyano(2-methoxyphenyl)methyl]-2-(morpholin-4-ylcarbonyl)cyclohexanecarboxamide,
 (1R,2R)-N-[Cyano(2-methoxyphenyl)methyl]-2-{[4-(4-fluorobenzyl)piperazin-1-yl]carbonyl}cyclohexane carboxamide,
- s (1R,2R)-N-[Cyano(2-methoxyphenyl)methyl]-2-(3,4-dihydroisoquinolin-2(1H)-ylcarbonyl)cyclohexane carboxamide,
 - (±) Trans-N-(cyanomethyl)-2-{[4-(4-fluorobenzyl)piperazin-1-yl]carbonyl}cyclohexanecarboxamide,
 - (±) Trans-N-[cyano(2-methoxyphenyl)methyl]-2-[(4-methylpiperazin-1-
- 10 yl)carbonyl]cyclohexanecarboxamide,
 - (1R,2R)-N-[Cyano(2-methoxyphenyl)methyl]-2-{[4-(4-fluorophenyl)piperazin-1-yl]carbonyl}cyclohexane carboxamide,
 - (1R,2R)-N-(4-Cyano-1-methylpiperidin-4-yl)-2-{[4-(4-fluorophenyl)piperazin-1-yl]carbonyl}cyclohexane carboxamide,
- and pharmaceutically acceptable salts thereof.

25

30

- 8. A compound of formula (I) as defined in any one of claims 1 to 7 for use in therapy.
- 9. A pharmaceutical composition which comprises a compound of the formula (I) as defined in any one of claims 1 to 7 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent or carrier.
 - 10. A method for producing inhibition of a cysteine protease in a mammal, such as man, in need of such treatment, which comprises administering to said mammal an effective amount of a compound of the present invention as defined in any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof.
 - 11. A method for producing inhibition of a cysteine protease in a mammal, such as man, in need of such treatment, which comprises administering to said mammal an effective amount of a compound as defined in any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof.

WO 2004/000825 PCT/SE2003/001080

23

12. A method for treating pain, such as neuropathic pain, in a mammal, such as man, in need of such treatment, which comprises administering to said mammal an effective amount of a compound as defined in any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof.

5